Peer reviewed article

A young woman with massive weight loss, neuropathy and cardiopathy

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In December 2000 a 45-year-old woman presented with a history of fatigue, light-headedness, nausea, vomiting, poor appetite, early satiety, diarrhoea and substantial weight loss (18 kg in the last 6 months). She had been complaining of progressive dysaesthesia and paraesthesia of the lower extremities for the previous eighteen months. On admission the physical examination revealed facial purpura particularly around the eyes (fig. 1), enoral submucosal bleeding spots and macroglossia (fig. 2). Blood pressure was 90/50 mm Hg and a symptomatic postural hypotension was detectable. Vibration sensation was reduced in the lower extremities and the Achilles tendon reflex was symmetrically impaired.

Laboratory tests showed hypoalbuminaemia of 21 g/l (30–52 g/l), total proteins 59.8 g/L (60–82 g/L) low iron of 6 mmol/l (6–30 mmol/l), transferrin saturation of 11% (15–50%) and an erythrocyte sedimentation rate of 10 mm/h. The following investigations were normal, negative or non-diagnostic: full blood count, liver function tests, lactate dehydrogenase (LDH), sodium, potassium, calcium, phosphate, creatinine, thyroid stimulating hormone (TSH), clotting factor X, prothrombin time and anticardiolipin antibodies.

Immunoelectrophoresis of the serum showed a monoclonal gammopathy of IgG lambda type (14.5 g/L). Proteinuria was 1.18 g/24 h (<0.15 g/l) consisting predominantly of monoclonal IgG lambda and free lambda light chains (0.05 g/24 h). Bone marrow aspirate and biopsy revealed 10–15% (in certain areas up to 30%) plasma cell infiltration.

An abdominal ultrasonography detected no abnormality. The gastro-oesophageal endoscopy revealed clearly reduced gastric motility with food retention and a moderate gastritis, positive for *H. pylori*. Radiographic studies of the upper gastrointestinal tract to demonstrate gut paresis were not performed. Biopsy of both stomach and rectum showed evidence of massive amyloidosis with predominant vessel-associated deposition (fig. 3) of immunohistological type IgG lambda (fig. 4).

An echocardiogram revealed cardiac involvement with concentrically thickened ventricular walls and restrictive physiology, as typically observed in light chains (AL)-amyloidosis. Left ventricular ejection fraction was 57%.

Parenteral nutrition was started and vomiting and nausea improved under metoclopramide treatment. *H. pylori* was eradicated with a standard triple therapy. Due to bladder retention the patient required catheterisation.

We performed chemotherapy with two initial cycles of doxorubicin and dexamethasone. Four weeks later the patient was discharged in good general condition. The treatment was continued with six cycles of oral melphalan and prednisone.

After a follow-up of 14 months the patient is in good general condition, body weight has increased by 7 kg and complete disappearance of the monoclonal gammopathy in the serum electrophoresis has been documented. Cardiac function has improved with a left ventricular ejection fraction of 70%.The peripheral neuropathy remains unchanged.

Due to perivascular deposition of AL-amyloid, vessels, especially the smaller ones, become frail and petechial bleeding is frequently observed creating the typical "raccoon-eyes" sign (fig. 1). Major bleeding is rare and is then associated with a secondary factor X deficiency. In general, weight loss is not a consequence of malabsorption or steatorrhea but is mainly due to the autonomic neuropathy with impairment of GI motility, pseudo-obstruction, nausea and vomiting [1, 2] with consequent malnutrition, as was probably the case in our patient. Vascular amyloid deposition causes luminal obstruction that sometimes leads to gastrointestinal infarction. Due probably to intestinal bacterial overgrowth, diarrhoea is present in many cases but overt steatorrhea and malabsorption are rare and mostly late events in the disease [1, 3]. Cardiac involvement with low output together with autonomic neuropathy are responsible for postural hypotonia.

As in other plasma cell dyscrasias, standard treatment consists of a combination of melphalan and prednisone [4, 5]. Compared to multiple myeloma, the response rate is generally lower, at approximately 30% [4] and again in contrast to multiple myeloma, the role of high dose chemotherapy for this disease is unclear. Some authors report a prolonged survival with intensive chemotherapy but no randomised studies have been reported so far and positive results of non-randomised studies could be due to a patient selection bias [6].

Although primary amyloidosis is a relatively rare disease, it should be included in the differential diagnosis of weight loss of unclear origin and treatment should always be considered as some patients will eventually benefit.

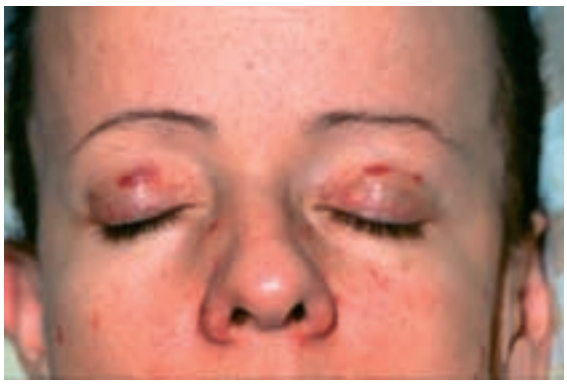


Figure 1

Spontaneous periorbital purpura, giving the typical "raccoon-eyes" sign.

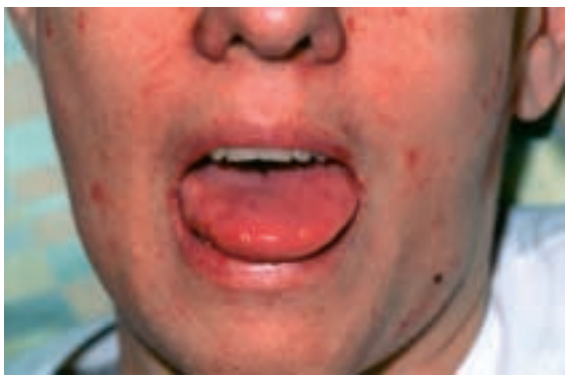


Figure 2

Macroglossia in amyloidosis. The tongue is frequently rimmed by the indentation of teeth.

The patient has given her informed consent for the publication of the figures.

Figure 3

Congo red staining showing massive perivascular amyloid deposition.

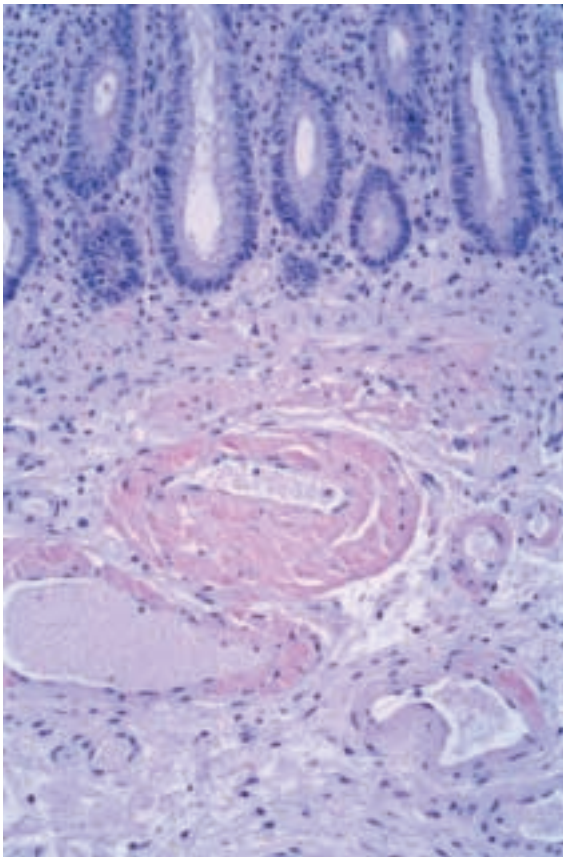
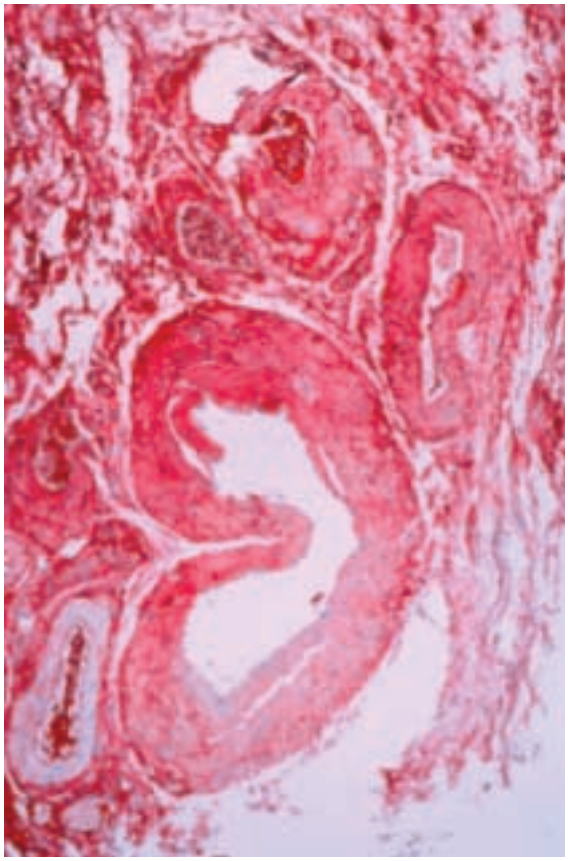


Figure 4

Immunohistochemical staining for lambda light chains.



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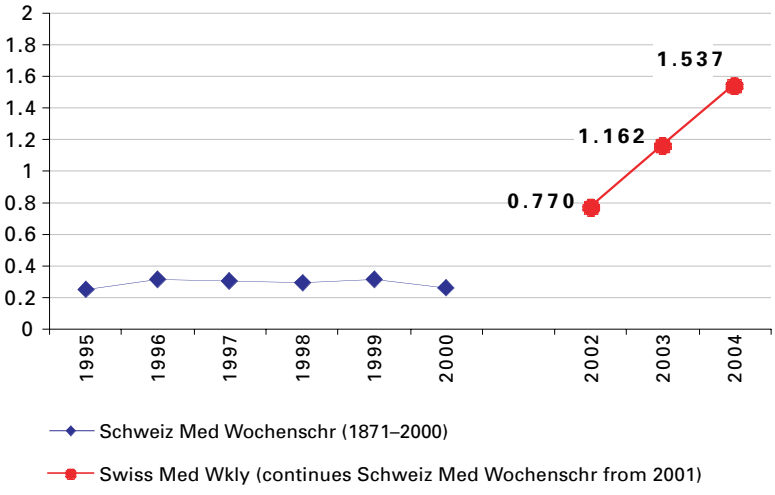

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